

REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance:

To understand why claim 35, as amended, is allowable over the prior art cited previously, it is necessary to understand the distinction between cell binding and cell infection for HSV. HSV particles bind to a variety of cell surface components via several different glycoproteins. gB and gC bind to heparan sulphate, gD binds to HVEM (HveA), nectin 1 (HveC), and nectin 2 (HveB). However, while binding is necessary for infection, it is not sufficient for infection. Apparently, gD undergoes a conformational change upon binding to one of its receptors, and interacts with gB, gH, and gL to fuse the viral envelope to the plasma membrane so that the capsid enters the cytoplasm. See the reviews by Garner and Spear, particularly "Structure of gD and interface with HVEM" on page 406 of Spear, and "Binding of the virus to the host cell surface" and "Fusion of the viral envelope to the host cell plasma membrane" on pages 1501-1504. Since the binding of gD to its cellular receptor is reduced by the claimed amendment, the effect of this reduced binding upon infection is not predictable, because there is no reasonable expectation that the fused peptide ligand would cause gD to assume the conformation required for fusion. Therefore, while there was a reasonable expectation that a cell-binding virus could be made having an altered gD with a peptide ligand and reduced native receptor binding, there was not the same reasonable expectation of functional fusion and infection. Without a reasonable expectation of infection, there was no reasonable expectation of killing the cell targeted by the peptide ligand.

In addition, as noted in the previous Office action, the closest prior art involved HSV with gC-ligand fusion protein. In Laquerre et al, the virus successfully bound to cells having the receptor for the ligand, but the virus did not successfully infect the cells. The virus instead entered lysosomes and was degraded. Again, this did not suggest a reasonable expectation of success for killing cells with HSV having an analogous gD-ligand fusion.

Since provisional double patenting rejections are the only rejections remaining, and since this application was filed earlier than the copending applications, the provisional double patenting rejections are hereby withdrawn. See MPEP 804 (I)(B)(1).

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is 571-272-0906. The examiner can normally be reached on varying dates and times; please leave a message.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1648

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/Mary E Mosher, Ph.D./
Primary Examiner, Art Unit 1648

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